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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/514,113

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Frank B. Dean

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EXAMINER

SISSON, BRADLEY L

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/514,113	Applicant(s) DEAN ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19, 21, 22 and 50-80 is/are pending in the application.
- 4a) Of the above claim(s) 50-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 21, 22 and 77-80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Claims 50-76 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on 09 January 2001.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-19, 21, 22, and 77-80 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,849,544 (Harris et al.) in view of US Patent 5,487,993 (Herrnstadt et al.).

6. Claim 1 is representative of the claimed invention and for convenience, claim 1 is reproduced below.

1. (Previously Presented) A method of reducing formation of artifacts in a nucleic acid amplification reaction, the method comprising
conducting a nucleic acid amplification reaction using a template-deficient oligonucleotide as a primer,
wherein the template-deficient oligonucleotide comprises one or more template-deficient nucleotides,
wherein the number and composition of template-capable nucleotides 3' of the template-deficient nucleotide closest to the 3' end of the template-deficient oligonucleotide is sufficient to allow the template-capable nucleotides 3' of the template-deficient nucleotide closest to the 3' end alone to effectively prime nucleic acid synthesis in the nucleic acid amplification reaction.

7. The aspect of what constitutes a "template deficient nucleotide" has become critical to the present rejection. Page 6, last paragraph, bridging to page 7 of the specification provides a definition:

Template-deficient nucleotides are selected from the group consisting of modified nucleotides, derivatized nucleotides, ribonucleotides, and nucleotide analogs. Preferred template-deficient nucleotides are modified nucleotides. Preferred modified nucleotides are abasic nucleotides. Template-deficient nucleotides include abasic nucleotides, nucleotides with an inverted base, fluoro substituted nucleotides, alkyl substituted nucleotides, nucleotides with a phenyl substituted ethers, nucleotides with substituted thioethers, nucleotides with phosphate esters, G-nucleotides, 2',3'-dideoxy nucleotides,

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ribonucleotides, nucleotides derivatized with biotin, nucleotides derivatized with amine, nucleotides derivatized with Hex, nucleotides derivatized with Tet, nucleotides derivatized with Fam, nucleotides derivatized with fluorescein, nucleotides derivatized with rhodamine, nucleotides derivatized with alkaline phosphatase, nucleotides derivatized with horseradish peroxidase, nucleotides derivatized with spacers, nucleotides derivatized with cholesteryl, nucleotides derivatized with DNP-TEG, nucleotides derivatized with psoralen cross-linkers, nucleotides derivatized with intercalating agents, and nucleotides derivatized with PNA conjugates. (Emphasis added.)

8. As seen above, the claim requires one to have at a minimum one template-deficient nucleotide in the oligonucleotide, and as defined, the template deficient nucleotide could be a nucleotide that has been derivatized with biotin.

9. Harris et al., column 3, bridging to column 4, teaches explicitly of using oligonucleotides as primes where the primer comprises a biotinylated nucleotide. Harris et al., column 4, first paragraph, and again at column 5, lines 37-41, teach using still other template-deficient nucleotides, identifying the use of fluorophores, and chelates. Such showings clearly meet the requirement that one employ a template deficient oligonucleotide, and are in stark contrast to assertions made by applicant's representative at pages 10-11 of their response of 07 March 2006.

10. Harris et al., has not been found to emphasize the complementarity of the 3' terminus and the number of template-competent nucleotides needed there to initiate primer extension.

11. Herrnstadt et al., column 6, teach a method of conducting nucleic acid amplification where the primer contains non-complementary nucleotides as well as complementary nucleotides, and that "the primer must contain at its 3' terminus a nucleotide sequence sufficiently complementary to non-randomly hybridize with its respective template strand.

12. Herrnstadt et al., column 6, bridging to column 7, reference Sommer et al., as disclosing that "primers having as little as a 3 nucleotide exact match at the 3' end of the primer is capable of specifically initiating primer extension products."

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13. Herrnstadt et al., column 11, bridging to column 12, disclose a plethora of labels that can be used in combination with their primers, including chemically modified bases, specifically identifying “biotin-containing groups, fluorescent compounds, and the like.” Such a showing is considered to meet the limitations of using template-deficient nucleotides in an oligonucleotide.

14. One of ordinary skill in the art at the time the invention was made would have been motivated to have combined the teachings of Herrnstadt et al., with that of Harris et al., so as to avoid non-functional primers, and thereby enhance the specificity and detectability of the amplification reactions.

15. In view of the combined and detailed teachings of Harris et al., and Herrnstadt et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to have incorporated any number of template deficient nucleotides in the 5' region of a primer so long as the 3' region was of sufficient length to allow for effective priming of the template strand, and to have used such a primer in a method of amplification. In view of the enhanced ability to immobilize amplicons, said ordinary artisan would have been amply motivated as such would have allowed for increased functionality of the method. In view of the wide application of modified primers to all forms of amplification, the ordinary artisan would have had a most reasonable expectation of success.

16. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-19, 21, 22 and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,849,544 (Harris et al.) in view of US Patent 5,487,993 (Herrnstadt et al.).

Response to argument

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17. At page 12 of the response argument is presented that Harris et al., does not “indicate that the biotin at the 5’ end of the primer would prevent the 5’ nucleotide from serving as a template for replication.”

18. The above argument has been fully considered and has not been found persuasive as the prior art is teaching one to use the very compounds recited in the instant application. Given that a compound and its properties are inseparable, it stands to reason that the same compound, used in the same manner claimed, would exhibit the same properties. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

19. Rejections and/or objections that appeared in the prior Office action and not repeated hereinabove have been withdrawn.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

23. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
24 May 2006